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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/653,812	09/01/2000	Haig H. Kazazian JR.	9596-23U3	6101

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EXAMINER
FALK, ANNE MARIE

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/653,812	KAZAZIAN ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/22/02, 8/5/02, and 11/21/02*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34,36-44,46,47 and 49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34, 36-44, 46, 47, and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 September 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/1/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Sequence Listing filed November 7, 2002 has been entered.

The amendment filed April 22, 2002 (hereinafter referred to as "the response") has been entered. Claims 34, 36-44, 46, 47, and 49 have been amended. Claims 35, 45, and 48 have been cancelled.

Accordingly, Claims 34, 36-44, 46, 47, and 49 remain pending in the instant application.

Drawings

The drawings are objected to for the reasons set forth on the Notice of Draftsperson's Patent Drawing Review (PTO-948) mailed 12/17/01 as part of Paper No. 5. New drawings must be submitted in response to this Office Action. Applicant may not request that any objection to the drawings be held in abeyance. See 37 CFR 1.85(a). See the Office Action Summary (PTO-326) mailed 12/17/01 which states that objections to the drawings will not be held in abeyance.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). Non-initialed and non-dated alterations were made to the residence, citizenship, and post office address of John Moran.

A newly executed declaration is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34, 36-44, 46, 47, and 49 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 2-6 of the Office Action mailed 12/17/01, and for further reasons as discussed herein, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a transgenic mouse comprising a specific retrotransposon, as well as a sperm cell obtained from a male transgenic mouse comprising said specific retrotransposon.

The specification fails to provide an enabling disclosure for the claimed transgenic mouse because the phenotype of a transgenic mouse is unpredictable. Thus, the specification does not teach how to use the claimed transgenic mouse.

At page 4 of the response, Applicants assert that the specification clearly teaches the generation of a transgenic mouse. However, for reasons of record, the existence of methods for making a transgenic mouse are not sufficient to enable the claimed mouse because the statute further requires that the specification must teach how to use the claimed mouse. In the absence of an appropriate phenotype, the skilled artisan would not know how to use the claimed transgenic mouse.

At page 5, paragraphs 1 and 2 of the response, Applicants assert that the specification teaches how to use the claimed transgenic animal and that a transgenic phenotype is disclosed and specified. Applicants argue that retrotransposons can be used to randomly disrupt genes through its random integration into the genome. Applicants argue that this will lead to disease states. However, the claims are not directed to disease models. On the contrary, the claims are directed to transgenic mice that have

no particular transgene-dependent phenotype. Clearly, any potential use of a transgenic mouse of the type claimed would depend on the particular gene that is disrupted, if any, as well as the specific nature of the disruption, and the phenotype that results from that particular disruption. However, the claims are not directed to transgenic mice that have a gene disruption, wherein said mice exhibit a specific phenotype as a consequence of that gene disruption. On the contrary, the claims are directed to mice that have no particular transgene-dependent phenotype. Applicants are arguing limitations that are not in the claims.

At page 5, paragraph 3 of the response, Applicants assert that a wild-type CFTR gene can be inserted into the genome of a transgenic mouse that has a mutated CFTR gene, thus alleviating the symptoms of a mouse that has cystic fibrosis. Applicants point to the specification at page 34, beginning at line 15, which does **not** describe that which Applicants contemplate in their response. The paragraph on page 34 simply states that **gene therapy** has been used in humans that have a mutated CFTR gene. With regard to Applicants newly contemplated use described in the response, first it is noted that treating an **induced disease** is not a patentable utility within the meaning of 35 U.S.C. 101, which requires a specific and substantial asserted utility. Inducing a disease only to come full circle by supplying the same gene that was disrupted, is not a use of the transgenic mouse of the invention. Second, it is noted that the specification **does not disclose** a transgenic mouse that hase a mutated CFTR gene. Third, the claims are not directed to a mouse that has a mutated CFTR gene. Fourth, given the unpredictability of phenotype in transgenic mice, for reasons of record, one of skill in the art would not know *a priori* the **phenotype** of a mouse having a mutated CFTR gene. Applicants are arguing limitations that are not in the claims.

At page 5, paragraph 4 of the response, Applicants assert that the discussion on page 6, lines 18-23 refers to "a disclosed and specified phenotype in the transgenic animal of the invention." It does not. The paragraph refers to gene therapy and does not in any way disclose a phenotype of a transgenic animal or even mention a transgenic animal. Applicants further refer to the specification at page 20, lines 6-18 for teaching "a disclosed and specified phenotype in the transgenic animal of the invention." Again, it

does not. On the contrary, the paragraph refers to gene therapy and DNAs that could be used in gene therapy. The cited section does not in any way disclose a phenotype of a transgenic animal or even mention a transgenic animal. At page 6, paragraph 1, Applicants conclude that "the disclosed and specified transgene dependent phenotype is alleviation of the disease state resulting from the genetic defect." However, the claims are not directed to gene therapy; the claims are directed to transgenic mice. The claims do not include administering a gene to an animal to alleviate a disease state. That would be gene therapy. The cited sections clearly do not disclose the **phenotype** of a transgenic mouse.

At page 6, paragraphs 5-8 of the response, Applicants argue that the transgenic mouse can be used to clone mouse genes. However, such a use does not constitute a **specific and substantial** asserted utility within the meaning of 35 U.S.C. 101 because such a use constitutes carrying out further research on the product made, i.e. the transgenic mouse. A **specific** utility is one that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention. Since all animals are a source of genes, such a use does not constitute a **specific** utility. A **substantial** utility is one that defines a real world use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a real world context of use are not substantial utilities. Research that involves studying the properties of the claimed product itself does not constitute a substantial utility. In this case, the utility is also not **substantial** because it constitutes carrying out further research on the claimed product itself.

The only utility asserted in the specification that rises to the level of a specific and substantial utility is the use of the transgenic mouse as a disease model. This utility is loosely asserted or implied in the specification where it refers to randomly integrating the L1 retrotransposon within the genome of an animal and where it states that the L1 retrotransposon is mutagenic (page 3, line 14). However, since the specification does not disclose a transgenic mouse having a disease phenotype, the skilled artisan would not know how to use the claimed transgenic mouse.

Thus, no utility rejection has been made in this case because the Examiner deems that at least one credible utility has been asserted in the specification, albeit one that is not enabled by the instant specification. Where Applicants argue utilities that do not rise to the level of a specific and substantial asserted utility within the meaning of 35 U.S.C. 101, whether enabled or not, such utilities will not be addressed with regard to their enablement. Only utilities that rise to the level of a specific and substantial asserted utility within the meaning of 35 U.S.C. 101 are considered under enablement.

While it is clear that Applicants wish to claim any disease model that can be generated by disruption of a gene in a transgenic mouse, the specification does not describe the **phenotype** of even a single mouse having a particular gene disrupted. Absent a particular phenotype, and given the unpredictability in the art, one would not know how to use the mice claimed, which have no particular phenotype.

At page 7, paragraph 5 of the response, Applicants state that the Examiner has argued that the **generation** of transgenic animals is unpredictable (emphasis added). This is highly inaccurate. On the contrary, the Examiner has acknowledged that **gene transfer** techniques are well-developed for a number of species. Nothing more than germline gene transfer is required to **generate** a transgenic animal. The unpredictability is the **phenotype** of the resulting transgenic animal, whether it is a mouse or some other species. Applicants dismiss all the references cited by the Examiner as not being applicable to the present claims because the present claims have been narrowed to claim only mice. However, the references apply equally to mice as to any other species. Clearly, when the skilled artisan cannot produce the desired disease phenotype in a transgenic mouse (see Mullins et al., 1989 and Taurog et al., 1988), the phenotype of transgenic mice is unpredictable.

At page 8, paragraph 1 of the response, Applicants assert that both Taurog and Hammer were able to achieve successful and predictable expression of a transgenic phenotype. On the contrary, the phenotypes observed were quite **unexpected** because the transgenic mouse did not produce the desired

HLA-B27-associated disease phenotype. How can this be considered an achievement of a "successful and predictable expression of a transgenic phenotype"? It is clearly a failure to produce the desired disease phenotype in the transgenic mouse upon expression of the transgene.

Given that the asserted utility for the instant invention is to produce disease models upon insertion of the transgene recited in the claims, the same problems can be expected to arise here. In view of the unpredictability of phenotype in the transgenic art, the lack of applicable working examples, and the limited guidance of the specification, one skilled in the art would have been required to engage in undue experimentation to determine how to use the claimed transgenic mice.

Thus, the rejection under 35 U.S.C. 112, first paragraph, is maintained.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your

questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER